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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/451,666	11/30/1999	TOSHIAKI ITO	07898-051001	9360

20985 7590 04/01/2002

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EXAMINER	
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ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 04/01/2002

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No. 09/451,666	Applicant(s) ITO ET AL.	
	Examiner BJ Forman	Art Unit 1634	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☒ The proposed amendment(s) will not be entered because:

   (a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

   (b) ☐ they raise the issue of new matter (see Note below);

   (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

   (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____.

3. ☐ Applicant's reply has overcome the following rejection(s): _____.

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☐ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:

   Claim(s) allowed: _____.

   Claim(s) objected to: _____.

   Claim(s) rejected: _____.

   Claim(s) withdrawn from consideration: _____.

8. ☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10. ☐ Other: _____

Advisory Action

1. This action is in response to papers filed18 March 2002 in Paper No. 26 in which claims 24-30 and 34-36 were amended and claim 21 was canceled. The amendments will not be entered because they raise new issues which would require further search and/or consideration or because they are not deemed to place the claims in better form for allowance.

The amendments to Claim 24 will not be entered because the amendments raise new issues (i.e. "wherein the binding agent and the plurality of probes are spotted with a pin or a tube") which would require further search and consideration. It is noted that rejected Claims 27 and 28 which depend from Claim 24 recite "wherein the mixture, the probe or the binding agent is spotted with a pin (tube)". The limitations in the alternative "the probe or the binding agent" differ in scope from amended Claim 24. Therefore, the limitations added to Claim 24 raise new issues and would require further search and consideration.

The amendments to Claims 25-30 and 34-36 will not be entered because they are not deemed to place the application in better form for allowance or appeal. The arguments regarding the previous rejections have been considered and are discussed below.

The previous rejections under 35 U.S.C. 102(e) and 35 U.S.C. 103(a) are maintained.

Response to Arguments

2. Regarding Claims 7 and 24:

Applicant argues that the method of Beattie et al does not comprises "spotting" even if "spotting" is given the broadest reasonable interpretation. The argument has been considered but is not found persuasive because, as stated in the previous Office Action, Webster's Ninth New Collegiate Dictionary (Merriam Webster, Inc. 1991, page 1141) defines "spotting" as to mark in a spot; to locate or identify a spot; to lie at intervals in or over; to place at intervals or

in a desired spot. The definitions provided by Webster encompass the method step of Beattie et al. wherein they place the binding agent at intervals; locate a spot for binding agent; or mark the binding agent in a spot. Given the broadest reasonable interpretation in view of well known definitions taught by Webster's, Beattie et al. disclose spotting the binding agent (Column 13, lines 51-62). Therefore, Beattie et al. disclose the method of making a biochip as claimed. Applicant further argues that Beattie flows a solution is flowed into pores to deliver a binding agent wherein Beattie's intention is to coat the entire pore including pore walls which differs from the claimed intention. The argument has been considered but is not found persuasive because while the surface of Beattie is porous, the method of Beattie comprises spotting binding agent and the probe and produces a biochip comprising a plurality of spots as claimed (Fig. 5 and 6).

Applicant argues that Beattie does not teach or suggest a method for making a biochip using a pin or a tube to spot a binding agent or a probe to a plurality of spots. The argument has been considered but is deemed moot in view of the fact that the argument addresses new limitations which have not been entered. Therefore the argument is irrelevant to the rejected claims.

3. Regarding Claims 6, 23, 25, 26, 28 and 29:

Applicant argues that the binding agent of Balch is the streptavidin film and differs from the instantly claimed binding agent wherein the binding agent is only provided on an area of the biochip where a probe is to be spotted. The argument has been considered but is not found persuasive because the claims and the specification broadly define "binding agent" as a "binding agent for binding probes to the plate" (page 4, second paragraph). The claims and the specification do not limit the "binding agent" to streptavidin and nothing in the claims or specification teaches that biotin is not a "binding agent". While streptavidin is a binding agent, a biotin-derivatized nucleic acid is also encompassed by the claimed "binding agent"

because biotin is an agent for binding probes to the plate or biochip. Therefore, the biotin-derivatized nucleic acid of Balch is encompassed by the broadly claimed "binding agent". Balch provides a mixture of binding agent and probe i.e. biotin-derived nucleic acid and the attached probe and they spot the mixture to a plurality of positions on the surface thereby producing a biochip as broadly claimed (Column 6, lines 1-24 and Column 18, lines 55-66).

4. Regarding Claims 6, 21, 23, 25-27 and 30-36:

Applicant argues that neither Martinsky nor TeleChem disclose a mixture of binding agent and probe to be spotted on a biochip or plate and neither disclose spotting a mixture of a binding agent and probe to a plurality of spots because the silane coating of Martinsky is their binding agent and the Micro-Spotting Solution of TeleChem does not comprise a binding agent. The argument has been considered but is not found persuasive because the claims and the specification broadly define "binding agent" as a "binding agent for binding probes to the plate" (page 4, second paragraph). The claims and the specification do not limit the "binding agent" to silane coating and nothing in the claims or specification teach that the "Micro-Spotting Solution" which contains charged components and provides a better quality microarray is not a "binding agent". While silane coating is a binding agent, a buffer containing charged components is also encompassed by the claimed "binding agent" because, as Martinsky teaches, the "Micro-Spotting Solution" is an agent for binding probes to the plate (Column 8, lines 51-58). Therefore, the Micro-Spotting Solution" of Martinsky is encompassed by the broadly claimed "binding agent".

5. Regarding Claim 7:

Applicant argues that because the silane coating of Martinsky is their binding agent, the biochip of Martinsky comprises binding agent on portions of the surface where there is not probe. Applicant further argues that TeleChem does not cure the defect in Matinsky because TeleChem does not teach or suggest methods for producing a biochip comprising spotting a mixture of binding agent and probe to a plurality of spots and the Micro-Spotting Solution does not contain a binding agent. Therefore, because Martinsky in combination with TeleChem do not teach or suggest spotting a mixture of binding agent and probe on a biochip, Claim 7 is not obvious by Martinsky as taught by TeleChem. The arguments have been considered but are not found persuasive for the reasons stated above regarding Claims 25 and 26 i.e. the claims and the specification do not limit the "binding agent" to silane coating and nothing in the claims or specification teach that the "Micro-Spotting Solution" which contains charged components and provides a better quality microarray is not a "binding agent". While silane coating is a binding agent, a buffer containing charged components is also encompassed by the claimed "binding agent" because, as Martinsky teaches, the "Micro-Spotting Solution" is an agent for binding probes to a plate (Column 8, lines 51-58). Therefore, the Micro-Spotting Solution" of Martinsky, which is not present where there is no probe, is encompassed by the broadly claimed "binding agent".

6. Regarding Claims 21, 24, 27 and 30-36:

Applicant argues that the binding agent of Martinsky is not spotted prior to the step of spotting the probes. The argument has been considered but is not found persuasive because the claims do not recited spotting the binding agent "prior to the step of spotting the probes". Claim 24 recites "spotting a plurality of probes onto the positions spotted in step (b)" which merely limits the location of the spotting but does not limit the sequence of binding agent and probe spotting. Therefore, the argument is not found persuasive because the argument

addresses limitations not in the claim. Applicant argues that the biochip of Martinsky comprises binding agent on portions of the surface where there is not probe. The argument has been considered but is not found persuasive as addressed above i.e. the claims and the specification do not limit the "binding agent" to silane coating and nothing in the claims or specification teach that the "Micro-Spotting Solution" which contains charged components and provides a better quality microarray is not a "binding agent". While silane coating is a binding agent, a buffer containing charged components is also encompassed by the claimed "binding agent" because, as Martinsky teaches, the "Micro-Spotting Solution" is an agent for binding probes to a plate (Column 8, lines 51-58). Therefore, the Micro-Spotting Solution" of Martinsky, which is not present where there is no probe, is encompassed by the broadly claimed "binding agent".

Applicant argues that TeleChem does not teach a binding agent is spotted prior to spotting the probe. The argument has been considered but is not found persuasive because the claims do not recited spotting the binding agent "prior to the step of spotting the probes". Claim 24 recites "spotting a plurality of probe onto the positions spotted in step (b)" which merely limits the location of the spotting but does not limit the sequence of binding agent and probe spotting. Therefore, the argument is not found persuasive because the argument addresses limitations not in the claim.

Applicant argues that the method of Beattie do not comprise spotting even if the term "spotting" is given its broadest reasonable interpretation. The argument has been considered but is not found persuasive for the reasons stated above in ¶ 2.

Applicant further argues that because Beattie and Martinsky/TeleChem teach different methods for producing a biochip, there is no motivation to modify the teachings of one with the other. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some

teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the binding agent spotting of Beattie to the spotting steps of Martinsky and to spot a binding agent onto the biochip prior to spotting the probe to thereby attach probes to pre-determine and confined regions efficiently as taught by Beattie (Column 4, lines 40-55).

7. Regarding Claims 28 and 29:

Applicant argues that Martinsky /TeleChem does not teach or suggest spotting a binding agent to a biochip. The argument has been considered but is not found persuasive as addressed above in ¶ 4. Applicant argues that Beattie does not teach or suggest spotting a binding agent as claimed. The argument has been considered but is not found persuasive as addressed above in ¶ 2. Applicant argues that Balch does not teach or suggest spotting a binding agent to a biochip. The argument has been considered but is not found persuasive as addressed above in ¶ 3. Therefore, Applicant argues, neither Martinsky/TeleChem, Beattie nor Balch alone or in combination teach or suggest each and every limitation of the claimed invention. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, it would have been obvious to one of ordinary skill in the art at the time

the claimed invention was made to apply the capillary tube spotting of Balch to the spotting methods of Martinsky/TeleChem and Beattie because capillary spotting permits small volume spotting with minimal evaporation or cross-contamination as taught by Balch (Column 12, lines 13-35). Therefore, the skilled practitioner in the art would have been motivated to apply the capillary tube spotting of Balch to the spotting of Martinsky/TeleChem and Beattie for the expected benefit of minimizing evaporation and cross-contamination as taught by Balch (Column 12, lines 13-35).

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:30 TO 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
Patent Examiner
Art Unit: 1634
March 27, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600